

PHARMACOLOGICAL MANAGEMENT OF NEUROPATHIC PAIN IN PRIMARY CARE

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PHARMACOLOGICAL MANAGEMENT OF NEUROPATHIC PAIN IN PRIMARY CARE

INTRODUCTION

Neuropathic pain is a symptom that develops as a result of damage to or dysfunction of the nervous system. Pain can be constant or intermittent and is usually described by the patient as one or more of the following; “burning”, “tingling”, “numb”, “shooting”, “stabbing”, “prickling”.

Central neuropathic pain is defined as ‘pain caused by a lesion or disease of the central somatosensory nervous system’. Examples of conditions that can cause this include stroke, spinal cord injury and multiple sclerosis. Peripheral neuropathic pain is defined as ‘pain caused by a lesion or disease of the peripheral somatosensory nervous system’ and can be a symptom of diabetic neuropathy, trigeminal neuralgia, herpes zoster infection (post-herpetic neuralgia) and chemotherapy-induced neuropathy. (NICE CG173, November 2013)

Neuropathic pain can be a symptom of a serious underlying disease e.g. malignancy and therefore any red flags or differential diagnoses must be investigated and excluded prior to initiating treatment.

SCOPE

This guideline provides prescribing recommendations for the pharmacological management of adults with neuropathic pain in a non-specialist setting.

GENERAL GUIDANCE

ASSESSMENT OF PATIENT

Use a reputable neuropathic pain questionnaire such as the **Leeds Assessment of Neuropathic Signs and Symptoms (LANSS) Pain Scale** (Appendix 1) or the **DN4 Questionnaire** (Appendix 2) together with a thorough medical consultation to assess for and document the severity of neuropathic pain. The baseline pain scales will help to evaluate whether the treatments, once initiated, are beneficial in improving the symptoms.

REVIEW OF TREATMENT EFFICACY

A treatment review date should be scheduled after starting treatment. See algorithm for adequate trial periods under each drug, however for some patients it may be better to schedule this in right at the start.

A 30 – 50% improvement in pain intensity and impact on lifestyle, daily activities (including sleep) and participation is considered to be “successful” treatment. Patients should be encouraged to maintain a healthy lifestyle and perform the recommended exercises to build strength, maintain flexibility as soon as they are able to, as this will provide the greatest benefit in the longer term.

RISK OF DEPENDENCE / ADDICTION

Patients should be advised that all oral medications in the neuropathic pain algorithm carry a risk of developing dependence (psychological or physical) when taken, particularly if they start taking the medication at more frequent intervals or at higher doses than prescribed. If they feel that they need to take the medication in this manner they must contact the prescriber.

The risk can be reduced by ensuring that the patient is regularly assessed by the prescriber and by gradually withdrawing and stopping medication where it is not effective. Patients should be counselled that medications that work initially can stop working in the longer-term so it is important that they alert the prescriber if they feel that their medication is no longer controlling the pain.

Patients should be advised that they should not share or loan their prescription medications to anyone else as they can cause serious adverse effects in people who take them without being assessed by a doctor and prescribed them.

EFFECTS OF NEUROPATHIC PAIN MEDICATION ON DRIVING AND OPERATING HEAVY MACHINERY

All oral medications in the neuropathic pain algorithm can affect the patient's ability to drive or operate heavy machinery when taken. Patients should be counselled that the effects may be particularly worse during the initiation period and during upward titration of the dose. Patients should be advised not to drive or operate heavy machinery if they feel, for example, that the medication is causing them to feel drowsy, dizzy, unable to concentrate or slower to react than usual. Patients and prescribers are advised to check the [DVLA website](#) for the latest information about the laws relating to drugs/medicines and driving.

NATIONAL INSTITUTE OF CLINICAL EXCELLENCE

The decision from NICE stakeholders, following the 2017 surveillance report, states that there was an insufficient volume of evidence to trigger an update to the NICE Clinical Guideline (CG 173) on the Management of Neuropathic Pain (2013).

NICE CG 173 recommends Amitriptyline (off label), duloxetine, gabapentin or pregabalin as safe and cost-effective options. NICE did not recommend one drug as clearly superior to others and advised that the choice of treatment should be made on an individual basis.

NICE does not make recommendations regarding the use of combined treatments because there is a lack of evidence for effectiveness, however the clinical development group noted that it may be more practical & more effective than switching treatment and may reduce adverse effects of the individual drugs.

NICE DOES NOT recommend the use of **anticonvulsants** for managing **low back pain without sciatica**.

NICE recommends that the following treatments SHOULD NOT BE USED in non-specialist settings unless advised by a specialist to do so. See table below:

- | | |
|--|--|
| - Cannabis Sativa Extract (Hospital-only) | - Topiramate |
| - Capsaicin Patch (Hospital-only) | - Venlafaxine |
| - Lacosamide | - Sodium Valproate (see MHRA alert) |
| - Lamotrigine | - Tramadol (long-term use) |
| - Levetiracetam | |
| - Morphine | |
| - Oxcarbazepine | |

Note: NICE recommends **tramadol** can be started in non-specialist settings only if acute rescue therapy is needed. For dosing recommendations, see current British National Formulary (BNF) guidelines.

LICENSING OF NEUROPATHIC PAIN MEDICATIONS

This guideline recommends using some medications off-licence (i.e. amitriptyline and capsaicin 0.025% cream). Prescribers are responsible for their decision to use medications off-licence and should be satisfied that it is in the best interest of the patient's needs. The patient should be informed and consent documented.

SUMMARY OF LICENSING STATUS OF MEDICINES IN NEUROPATHIC PAIN	
Amitriptyline	Not currently licensed for neuropathic pain, but use is supported by NICE CG173
Gabapentin	Licensed for peripheral neuropathic pain
Pregabalin	Licensed for peripheral and central neuropathic pain
Duloxetine 30mg & 60mg strengths ONLY	Licensed for diabetic peripheral neuropathic pain
Capsaicin cream 0.075%	Licensed for post-herpetic neuralgia after open skin lesions have healed and painful diabetic peripheral polyneuropathy
Capsaicin cream 0.025%	Licensed for symptomatic relief of pain associated with osteoarthritis. Not licensed for neuropathic pain
Carbamazepine	Licensed for trigeminal neuralgia only
Lidocaine 5% plaster	Licensed for post-herpetic neuralgia only

NEUROPATHIC PAIN TREATMENT ALGORITHM

* Please note that dosing advice is correct at the time of writing but this document should be used in combination with current BNF and Summary of Product Characteristics (SPC) dosing guidance.

ALL NEUROPATHIC PAIN (excluding Trigeminal Neuralgia)

Unless contraindicated, regular **Paracetamol 1g FOUR TIMES A DAY** is recommended to be used concurrently throughout all the steps of the treatment as it may have a synergistic effect as well as exerting its own analgesic properties.

STEP 1. Amitriptyline (note: this is an unlicensed indication for TCAs)

Patient Information Leaflet can be found [here](#).

Information on exposure in pregnancy available [here](#)

Average cost of treatment approx. £2/month.

- **Start at 10 – 25mg in the evening (6 – 8pm)**, increase by 10 – 25mg every 3 – 7 days according to effect & tolerability

- **Usual Therapeutic Dose Range:** 25 – 75mg in the evening

There is limited evidence of effectiveness of doses larger than 75mg (use only on the advice of pain services)

- **Duration of adequate trial:** 6 – 8 weeks (allow 2 weeks at the maximum tolerated dose)

- **Do not stop abruptly** Reduce gradually by 10 – 25mg over 4 weeks or longer if withdrawal symptoms occur.

- **Contraindicated** in arrhythmias, heart block, severe liver disease, recent MI & manic phase of bipolar disorder.

STEP 2: GABA ANALOGUES

- Pregabalin and Gabapentin are structurally and pharmacologically related. If the pain does not respond to one or the other, stop and try a different agent (e.g. Amitriptyline). There is some evidence that if a patient is refractory or gets an insufficient response from gabapentin for their neuropathic pain, they might gain some benefit from pregabalin even though their mode of action is similar (Markman et al. 2017).
- [Public Health England](#) published advice for prescribers in 2014 about the risks of misuse and addiction of both gabapentin & pregabalin. Both are subject to diversion as they are “currency” in prisons and have a high “street” value. Hence both agents will shortly be given a Schedule 3 Controlled Drug status (in approximately April 2019) to avoid potential for abuse (for its own euphoric effects but also its use as an adjunctive substance with other drugs of abuse).
- Although there is an [MHRA alert](#) specifically for sodium valproate/valproic acid in females of childbearing potential, it may be pertinent to have discussions about effective contraception in females using other antiepileptic drugs e.g. gabapentin or pregabalin (also for other indications such as neuropathic pain).

Pregabalin

Patient Information Leaflet can be found [here](#).

Information on exposure of in pregnancy available [here](#)

Average cost of treatment approx. £6/month

Prescribe generically

- **Start at 75mg twice daily**, titrate upwards until efficacy achieved or not tolerated (see Table 1 for information on titration). **Reduced doses required in renal impairment** (see page 7).

- **Usual Therapeutic Dose Range:** 150 – 600mg daily in divided doses. SPC & BNF specify this can be two to three divided doses. However, in practice, twice daily dosing is most common.

- **Duration of adequate trial:** 3 – 8 weeks for titration (allow 2 weeks at maximum tolerated dose)

- **Do not stop abruptly.** See page 7 for instructions on discontinuation.

OR Gabapentin

Patient Information Leaflet can be found [here](#).

Information on exposure of in pregnancy available [here](#)

Average cost of treatment is approx. £4/month

- **Start at 300mg at night**, titrate upwards by 300mg a week until efficacy achieved, max dose reached or not tolerated. Faster titration may be appropriate for individual patients. **Reduced doses required in renal impairment** (see page 7).
- **MHRA Safety Warning**: Rare risk of respiratory depression (see page 8)
- **Usual Therapeutic Dose Range**: 300mg – 3600mg daily in three divided doses.
- **Duration of adequate trial**: 3 – 8 weeks for titration (allow 2 weeks at maximum tolerated dose).
- **Do not stop abruptly**. See page 7 for instructions on discontinuation.

STEP 3: Duloxetine (1st line in diabetic neuropathy)

Patient Information Leaflet can be found [here](#).

Information on exposure in pregnancy available [here](#).

Average cost of treatment is approx. £4/month.

- **Start at 60mg daily** (a 30mg starting dose may be appropriate for some patients). Increase to 60mg twice daily if needed. **Avoid if CrCl <30ml/minute** and **avoid in liver disease** resulting in hepatic impairment.
- **MHRA Safety Warning**: Risk of suicidal ideation (see page 9). Monitor for signs of suicidal ideation/ worsening depression.
- **Duration of adequate trial**: 8 weeks (allow at least 4 weeks at maximum tolerated dose)
- **Do not stop abruptly**. Decrease dose gradually over at least 1 – 2 weeks

STEP 4: Combination Treatment Useful if there is a partial response to two agents from different classes but where dose titrations are limited due to issues with tolerability. The most common combinations are **GABA ANALOGUE + AMITRIPTYLINE** OR **GABA ANALOGUE + DULOXETINE**

TOPICAL TREATMENTS (Can be used at any STEP where oral treatment is not tolerated/ suitable)

Consider **capsaicin cream** for patients with **localised neuropathic pain** who wish to avoid, or who cannot tolerate oral treatments.

Patient Information Leaflet available [here](#).

(Note: the use of capsaicin 0.075% for diabetic neuropathy should only be used under the supervision of a specialist).

Cost of 1x45g tube 0.025% is £18. Cost of 1x45g tube 0.075% is £15.

- **Dose**: Apply a pea size amount of the 0.075% strength sparingly three to four times daily for 6 – 8 weeks. Do not use on broken skin. Avoid contact with eyes and mucous membranes.
- **Practical Tips**: If 0.075% is not tolerated then try again, starting with the milder 0.025% strength (off-label use) and increase if tolerated to the 0.075% strength. Although some people use gloves when applying, capsaicin can diffuse through latex gloves. Wash hands thoroughly after application unless hands are the area to which application is being made, in which case wash after 30 minutes. If application is to the feet, they should be covered to avoid contaminating the floor.
- **Duration of adequate trial**: Pain relief increases with continuing. There is no clinical trial data for use longer than 8 weeks.

TREATMENT OF POST- HERPETIC NEURALGIA (associated with previous herpes zoster infection)

Treat initially with standard oral therapies as per **Steps 1 – 4** and/ or **topical capsaicin** (unless contra-indicated or not tolerated).

If standard therapies fail, or lead to intolerable side effects, consider **lidocaine 5% medicated plasters**. Prescribe as the brand **RALVO®**. Patient Information Leaflet available [here](#). The cost of 30 plasters is £60.

Prescribe a trial of **2 weeks** initially and then review for effectiveness before the medication is continued as a repeat prescription. **Lidocaine plasters are approved for primary care initiation only when used to treat post-herpetic neuralgia.**

REVIEWING TREATMENT EFFICACY

- Titrate medications to maximum tolerated dose and measure the response by assessing the effect of the medication after the suggested trial periods, usually within **6 – 8 weeks** of initiation against the baseline neuropathic pain score and/or baseline function.
- At each stage, if a 30 – 50% improvement in pain and/or function is **not** demonstrated after the suggested period of adequate trial, **or** if the medication is not tolerated, then gradually withdraw and stop before moving to the next appropriate step (see page 7 for specific information around the titration and discontinuation specific to GABA Analogues).
- At each stage re-check for red flags and re-evaluate diagnosis.

WHEN TO REFER TO A SPECIALIST PAIN SERVICE

- If there is **<30%** improvement on pain symptoms and/or function, upon using the algorithm STEPS 1 to 4.
- If patient is complaining of recurring episodes of inadequate relief despite initially demonstrating a 30 – 50% improvement in pain symptoms and/ or function.
- At any time, if there is concern around dependence or abuse of prescriptions, or if there is a strong psychosocial component to the pain symptoms.

TREATMENT OF TRIGEMINAL NEURALGIA

Use **Carbamazepine 1st line**

Start at 100mg twice daily (Prescribe generically. Prescribe immediate release preparation). The Summary of Product Characteristics (SPC) and BNF recommend increasing gradually according to response with a usual dose of 200 mg 3 – 4 times a day. (MR preparations may be useful at night if the patient experiences breakthrough pain).

Monitoring: FBC, U&Es and LFTs at baseline and repeat periodically. Continue monitoring patient for symptoms of blood disorder (e.g. fever, sore throat etc.)

Not advised for use in moderate to severe renal impairment. If there is inadequate response or treatment is not tolerated consider early referral to a specialist pain or condition specific service.

GABA ANALOGUES

PREGABALIN

Dose titration: titration recommendations are based on the BNF and SPC. The regimen should be tailored to each individual patient and amended according to tolerance.

Table 1. Pregabalin Titration Regimen. Prescribe generically.

	Day 1, 2, 3	Day 4, 5, 6	Day 7, 8, 9	Day 10 (if necessary)
Morning	75mg	75mg	150mg	300mg
Night	75mg	150mg	150mg	300mg

MAXIMUM dose: Can be titrated up to **600mg/day**

DISCONTINUATION: Local guidance suggests reducing by 25 – 50mg a week until stopped. For those who are likely to be more susceptible to withdrawal e.g. those on high doses, elderly/frail, prescribed >12-months, reduce by 25mg a week. PHE recommends reducing the daily dose at a maximum of 50 – 100mg per week. The SPC suggests discontinuing gradually over a minimum of one week.

Table 2. Dose Reduction Required In Renal Impairment (as per SPC)

<https://www.medicines.org.uk/emc/product/5539>

CrCl (ml/min)	Starting dose	Maximum Dose
≥ 60	75mg BD	300mg BD
≥ 30 - < 60	25mg OM + 50mg ON	150mg BD
≥ 15 - < 30	25mg – 50mg ON	75mg BD
< 15	25mg ON	75mg ON

PREGABALIN can cause QT prolongation

NOTE: Pregabalin is “flat priced” across the dose ranges, therefore increase the strength of the capsule rather than simply increasing the number taken.

GABAPENTIN

Dose titration. The below regimen is as per local guidance but the BNF and SPC suggest an accelerated regimen. In practice, this is limited by side-effects and should be reserved for fit, healthy adults with a clear understanding of the titration and side effects.

Table 3. Gabapentin Titration Regimen (start at 100mg and increase proportionally in elderly or frail patients i.e. those likely to be susceptible to side-effects)

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Morning		300mg	300mg	300mg	300mg	600mg
Midday			300mg	300mg	600mg	600mg
Night	300mg	300mg	300mg	600mg	600mg	600mg

MAXIMUM dose: Can be titrated up to **3600mg/day**

DISCONTINUATION: Local guidance suggests reducing by 300mg a week until stopped. For those who are likely to be more susceptible to withdrawal e.g. those on high doses, elderly/frail, prescribed >12-months, reduce by 100mg a week in patients. PHE recommends reducing the daily dose at a maximum rate of 300mg every 4 days. The SPC suggests discontinuing gradually over a minimum of one week.

Table 4. Dose Reduction Required In Renal Impairment (as per SPC)

<https://www.medicines.org.uk/emc/product/5003>

CrCl (ml/min)	Total daily dose
≥ 80	900 – 3600 mg/day
50 - 79	600 – 1800 mg/day
30 - 49	300 – 900 mg/day
15 - 29	150 (given as 300mg alt days) – 600 mg/day
< 15	150 – 300mg/day and reduce daily dose in proportion to CrCl e.g. patients with CrCl < 7.5ml/min should receive half the daily dose of a patient with CrCl 15ml/min

MHRA/CHM advice Oct 2017: Rare risk of severe respiratory depression in adults and children, even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants and elderly people might be at higher risk of severe respiratory depression. Report any suspected adverse reactions at the [MHRA Yellow Card](#) website.

GENERAL PRESCRIBING POINTS

- Pregabalin and gabapentin can cause **weight gain**, which should be taken into consideration when selecting therapy for certain people e.g. patients with diabetes
- Both can be used in combination with amitriptyline or duloxetine (if there has been a partial response to either or both treatments)
- NICE **DOES NOT recommend the use of anticonvulsants** for managing **low back pain without sciatica**. A systemic review of 8 randomised controlled trials assessing the effects of gabapentinoids, in adults with chronic lower back pain, found that Gaba Analogues provide non-significant improvement in low back pain compared to placebo. Gaba analogues were associated with more adverse effects.
<https://discover.dc.nih.ac.uk/portal/article/4000857/two-nerve-drugs-are-not-suitable-for-treating-long-term-low-back-pain>

REVIEW OF TREATMENT

Where possible the patient should have ownership of the titration process and be given sufficient information and support to do this. They should also be advised that where the medication is **not showing benefit**, it will need to be **gradually reduced and stopped**.

Patients should be advised of side-effects including **drowsiness**, which may **affect their ability to drive** and how these can be managed or reduced e.g. by taking the largest dose at night and by slowing the titration process if needed. They should be informed that this medication carries a risk of dependence, particularly when taken in excess of what is prescribed and when not reviewed regularly for efficacy.

Patients should be advised that following a **maximum of 12 months of treatment, a trial reduction and withdrawal** may be necessary to determine if the medication is still having the desired effect and whether it is necessary to continue. It should be explained that this may help to reduce the risk of dependence.

DULOXETINE

Can be considered 1st line for patients with diabetic neuropathy.

Contraindicated for use:-

- with non-selective irreversible monoamine oxidase inhibitors (MAOIs)
- With potent CYP1A2 (liver cytochrome P450 isoenzyme) inhibitors e.g. fluvoxamine or ciprofloxacin;
- in liver disease resulting in hepatic impairment;
- in severe renal impairment (CrCl < 30ml/min);
- In patients with uncontrolled hypertension.

MHRA Advice 2007: Due to reported cases of suicidal ideation and suicidal behavior during treatment with duloxetine or shortly after stopping treatment, patients should be reviewed every 3 months for assessment of effectiveness of treatment and signs of depression/suicidal ideation.

TAPENTADOL

Tapentadol Modified-Release Tablets (Palexia®) is a strong opioid and a noradrenaline reuptake inhibitor for **initiation by the specialist pain services only**. In South West London CCGs Tapentadol will remain a hospital-only drug with the EXCEPTION of Wandsworth, Merton and Sutton CCGs.

Although Tapentadol is licensed for use in neuropathic pain, the NICE surveillance report 2017 found limited evidence for the use of Tapentadol and judged it to be insufficient to trigger an update to NICE CG 173 guideline. There is generally limited evidence for the use of opioids in the treatment of neuropathic pain, however there may be patients who have a mixed pain presentation or who have been historically prescribed strong opioids for their pain management. **Chronic Pain specialists will be restricting the use of Tapentadol to patients who are on high doses of opioids due to historical prescribing**, with a management plan to reduce their current opioid burden.

In Wandsworth, Merton and Sutton CCGs the pain specialist will initiate and provide the first 8 weeks of Tapentadol MR after which they will assess the patient for response and adverse effects. If the treatment is to be continued, the specialist will prescribe a further 4 weeks of Tapentadol (total 12 weeks supply) and the transfer of care documents, which includes a detailed medication plan will be sent to the GP. This will allow time for any concerns or questions to be raised by the GP and addressed by the specialist, before another prescription is due to be issued in primary care to the patient. **Patients who are started on Tapentadol that are already on other strong opiates must have a plan to reduce their concurrent opioid burden, as instructed in the medication plan.**

See **Appendix 3** for the Tapentadol Transfer of Care Protocol and **Appendix 4** for the Tapentadol MR Medication Plan and GP Information Sheet.

If there are any concerns that the Medication Plan and GP Information sheet does not contain sufficient information to take over prescribing, this should be alerted to the named contact on the sheet. If there is any concern that the patient is not engaging with the medication plan then this must be alerted to the named contact on the sheet.

LIDOCAINE 5% (700mg) PLASTERS (Ralvo® and Versartis®)

Lidocaine plasters are licensed for the treatment of post-herpetic neuralgia (PHN), however, the annual expenditure in 2016 across the whole of England was £19,295,030. The 2017-18 expenditure on lidocaine plasters was **£171,240** in Wandsworth CCG and **£112,534** in Merton CCG. Local primary care audit work (2017-18) has shown that this is attributed to a widespread off-label use in the management of chronic non-malignant pain, particularly low back pain. Audit data showed that there were similar numbers of patients that were initiated in primary care as were initiated in secondary care.

A Cochrane Review (2014) found no evidence from good quality randomised controlled studies to support the use of topical lidocaine to treat neuropathic pain, although individual studies indicated that it was effective for relief of pain. <http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD010958.pub2/full>

In 2017, NHS England included Lidocaine plasters under the category of “Low clinical effectiveness/ Lack of robust evidence of clinical effectiveness” in their publication of “Items Which Should Not be Routinely Prescribed in Primary Care – Guidance for CCGs”. NHSE recommends the following:

- Advise CCGs that prescribers in primary care should not initiate plasters for any new patient (with the **EXCEPTION** of patients who have been treated in line with NICE CG173 but are still experiencing pain associated with a previous herpes zoster infection i.e. PHN)
- Advise CCGs to support prescribers in de-prescribing lidocaine plasters in all patients (with the exception of the above PHN patients)
- Advise CCGs that if, in exceptional circumstances, there is a clinical need for lidocaine plasters to be prescribed in primary care, this should be undertaken in cooperation with a multidisciplinary team and/or other healthcare professional

Full details available at <https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/>

- **Place in Therapy:** Patients with PHN should initially be managed as per the treatment algorithm. Where this is inadequate, contraindicated or intolerable, lidocaine plasters may be initiated in primary care. Refer to the [SWL position statement on prescribing of Lidocaine plasters](#).

- **Name of Product:** Prescribe by brand **RALVO®** (£60 for 1 month treatment at 1 plaster per day)

- **Dose:** The painful area should be covered with the lidocaine plaster once daily for up to 12 hours within a 24 hours period. Use the least number of plasters required for effective treatment. The plasters may be cut into smaller sizes with scissors (prior to removal of the release liner) in order to minimise wastage, when applying to areas substantially smaller than the plaster size. **In total, not more than three plasters should be used at the same time.**

- **Other Instructions for use:** Each plaster must be worn no longer than 12 hours. The subsequent plaster-free interval must be at least 12 continuous hours. The plaster must be applied to the skin immediately after removal from the sachet and following removal of the release liner from the gel surface. Hairs in the affected area must be cut off with a pair of scissors (not shaved).

- **Review:** Treatment outcome should be re-evaluated 2 – 4 weeks after initiation and the plasters should be discontinued if they do not demonstrate a 30 – 50% improvement in baseline pain scores and/or function. If they demonstrate efficacy then review at 6 – 12 monthly intervals to assess on-going need. Long-term clinical studies showed that the number of plasters used decreases over time. Therefore at each review there should be a discussion around whether the amount of plasters applied can be reduced (if only on one plaster then consider cutting in half), or if the plaster-free period can be extended (e.g. from 12-hours to 24 hours and so on).

- **Discontinuation:** **Patients receiving lidocaine plasters for indications other than PHN need to be reviewed with a view to being discontinued if there are no clear exceptional circumstances for prescribing.** Patients requiring a withdrawal of lidocaine plasters should be advised to remove the plaster for ONE week. If the burning or tingling sensation returns then trial any non-medicated plaster as a barrier (can be purchased from pharmacies), which will act as a barrier between the skin and clothing to reduce sensitisation by rubbing of clothes. Alternatively try a mentholated plaster (e.g. **SALONPAS** which can be purchased from pharmacies) to cool and soothe the area. Other cooling and soothing products may be available – seek advice from the pharmacist.

REFERENCES

NICE CG173. Neuropathic Pain Management in adults: Pharmacological management in non-specialist settings. Accessed via <https://www.nice.org.uk/guidance/cg173>

BNF Accessed in-line via Medicines Complete <https://www.medicinescomplete.com/mc/bnf/current/>

CKS Neuropathic Pain Scenario <https://cks.nice.org.uk/neuropathic-pain-drug-treatment#!prescribinginfosub>

Duloxetine SPC <https://www.medicines.org.uk/emc/product/3880>

Pregabalin SPC <https://www.medicines.org.uk/emc/product/1761>

Gabapentin SPC <https://www.medicines.org.uk/emc/product/5003>

MHRA Duloxetine <https://www.gov.uk/drug-safety-update/duloxetine-marketed-as-cymbalta-and-yentreve-for-different-disorders>

MHRA Gabapentin <https://www.gov.uk/drug-safety-update/gabapentin-neurontin-risk-of-severe-respiratory-depression>

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Effects of Pregabalin in Patients with Neuropathic Pain Previously Treated with Gabapentin: A Pooled Analysis of Parallel-Group, Randomized, Placebo-controlled Clinical Trials. [John D. Markman MD](#) et al. Pain Practice.17, 6, July 2017 <https://onlinelibrary.wiley.com/doi/abs/10.1111/papr.12516>

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

Name Date

This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE

■ Think about how your pain has felt over the last week.

■ Please say whether any of the descriptions match your pain exactly.

1. Does your pain feel like strange, unpleasant sensations in your skin?

Words like pricking, tingling, pins and needles might describe these sensations.

a) NO – My pain doesn't really feel like this (0)

b) YES – I get these sensations quite a lot (5)

2. Does your pain make the skin in the painful area look different from normal?

Words like mottled or looking more red or pink might describe the appearance.

a) NO – My pain doesn't affect the colour of my skin (0)

b) YES – I've noticed that the pain does make my skin look different from normal (5)

3. Does your pain make the affected skin abnormally sensitive to touch?

Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.

a) NO – My pain doesn't make my skin abnormally sensitive in that area (0)

b) YES – My skin seems abnormally sensitive to touch in that area (3)

4. Does your pain come on suddenly and in bursts for no apparent reason when you're still?

Words like electric shocks, jumping and bursting describe these sensations.

a) NO – My pain doesn't really feel like this (0)

b) YES – I get these sensations quite a lot (2)

5. Does your pain feel as if the skin temperature in the painful area has changed abnormally?

Words like hot and burning describe these sensations.

a) NO – I don't really get these sensations (0)

b) YES – I get these sensations quite a lot (1)

Leeds Assessment of Neuropathic Symptoms and Signs (continued)

B. SENSORY TESTING

Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pin-prick threshold (PPT).

1. Allodynia

Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.

- a) NO – Normal sensations in both areas (0)
- b) YES – Allodynia in painful area only (5)

2. Altered pin-prick threshold

Determine the pin-prick threshold by comparing the response to a 23-gauge (blue) needle mounted inside a 2ml syringe barrel placed gently onto the skin in a non-painful and then painful areas.

If a sharp pin prick is felt in the non-painful area, but a different sensation is experienced in the painful area, eg. none/ blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present.

If a pinprick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.

- a) NO – Equal sensation in both areas (0)
- b) YES – Altered PPT in painful area..... (3)

SCORING:

Add values in parentheses for sensory description and examination findings to obtain overall score.

TOTAL SCORE (maximum 24).....

If score < 12, neuropathic mechanisms are unlikely to be contributing to the patient's pain.

If score ≥ 12, neuropathic mechanisms are likely to be contributing to the patient's pain.

APPENDIX 2: DN4 QUESTIONNAIRE

Interview Of The Patient

Question 1: Does the pain have one or more of the following characteristics?

	Yes	No
Burning		
Painful Cold		
Electric Shocks		

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

	Yes	No
Tingling		
Pins and Needles		
Numbness		
Itching		

Examination Of The Patient

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

	Yes	No
Hypoesthesia to touch		
Hypoesthesia to prick		

Question 4: In the painful area, can the pain be caused or increased by:

	Yes	No
Brushing		

TO COLLATE:

- Score 1 to each **YES** answer
- Score 0 to each **NO** answer
- If the score is 4 or higher then the pain is **likely** to be **neuropathic** pain.
- If the score is less than 4 then the pain is **unlikely** to be neuropathic pain.

APPENDIX 3: TAPENTADOL MR MEDICATION PLAN AND GP INFORMATION SHEET

Your patient has started taking **tapentadol**, a strong opioid, for the management of pain. Response to treatment has now been assessed after 8 weeks of treatment and the patient has been given a further 4 weeks supply. This medication plan is intended to support a transition to GP prescribing.

Brief description of the drug
Class: Tapentadol MR (Palexia® SR) is a strong opioid (acting primarily through opioid μ -receptor agonism) and noradrenaline reuptake inhibitor in a modified release formulation
St George's approved indications: Under the direction of a specialist pain service, tapentadol is indicated in selected cases of acute and chronic pain that have not responded to conventional opioid therapy.
Adverse effects: The adverse effects of tapentadol are similar to those of conventional opioids, including nausea and vomiting (particularly in initial stages), constipation, dizziness and somnolence. At higher doses, it may cause respiratory depression and reduced consciousness.
Significant interactions: Due to the effects of tapentadol on synaptic neurotransmitter concentrations, caution must be exercised in its co-prescription with other agents that affect synaptic function. The additive effects on synaptic noradrenaline or serotonin concentrations may cause sympathetic (e.g. hypertensive crisis) or serotonergic reactions (e.g. tachycardia, hypertension, hyperthermia, altered mental state), respectively. Co-prescription with monoamine oxidase inhibitors must therefore be avoided (risk of hypertensive crisis), and caution must be exercised in its co-prescription with other antidepressants (risk of serotonergic toxicity). Caution must also be exercised when considering co-prescription with drugs that depress consciousness or are strong hepatic enzyme inducers .
Monitoring: The monitoring requirements for tapentadol are similar to those for other strong opioids. *Aim is to reduce existing high opioid requirements*

Tapentadol medication plan			
Name	Address	GP name and address	Responsible pain team
DOB			<input type="radio"/> Inpatient pain team <input type="radio"/> Chronic pain team <input type="radio"/> Palliative care
MRN			Pain consultant
Diagnosis and trust-approved indication/place in therapy for tapentadol			
Diagnosis			
Indication for tapentadol <input type="checkbox"/> Severe chronic pain <input type="checkbox"/> Moderate to severe acute pain	Place in therapy for tapentadol <input type="checkbox"/> Pain with a neuropathic component that has not been adequately relieved by conventional anti-neuropathic pain agents AND conventional strong opioids (morphine or oxycodone), or these are not tolerated <input type="checkbox"/> Pain without a neuropathic component that has not been adequately relieved by conventional strong opioids (morphine or oxycodone), or these are not tolerated		
Initial tapentadol treatment and response <i>(Initial 8-week supply to be prescribed by specialist pain team)</i>			
Date tapentadol commenced	Date of review	Response at 8 weeks <input type="checkbox"/> Full relief <input type="checkbox"/> Partial relief	Adverse effects experienced to date and their management
Continuation of tapentadol treatment <i>(A further 4-week supply to be prescribed by specialist pain team to support transition to primary care)</i>			
Formulation and route Tapentadol prolonged-release tablets (Palexia® SR) to be taken by mouth		Dosage regimen	<input type="checkbox"/> Tick to confirm patient has been issued at least a TOTAL of 12 weeks of Tapentadol (initial 8-weeks plus a further 4-weeks) prior to transfer from pain specialist to GP.
Guidance for dosage titration and target dose <i>(including recommended dosage increments/decrements and interval between dosage changes)</i>			
Anticipated duration of therapy and/or criteria for stopping			
Additional notes			
Specialist pain team follow-up arrangements and sources of advice			
Follow-up clinic and interval		Pain team contact details for advice on this medication plan	
Completed by		Signature	Date

APPENDIX 4: PROTOCOL FOR THE USE OF TAPENTADOL MR (PALEXIA® SR) IN ACUTE AND CHRONIC PAIN

Brief Description of Drug: Tapentadol MR (Palexia® SR) is a **strong opioid** (acting primarily through opioid μ -receptor agonism) and a **noradrenaline reuptake inhibitor** in a modified-release (MR) formulation. Under the direction of a specialist pain team (the inpatient pain team, chronic pain team or palliative care, as appropriate for the patient and setting of care), it is an option for analgesia in selected patients with acute or chronic pain, who have not responded to conventional opioid therapy.

Trust Approved Indications:

In adults with **severe chronic pain** and **moderate to severe acute pain** in whom:

- 1) conventional opioids have failed to provide adequate pain control and/or are not tolerated; and/or
- 2) a neuropathic pain component cannot be excluded (subject to the *Place in Therapy* limitations; see below)

Place in Therapy:

- 1) **in pain with a neuropathic component:** under specialist direction from the pain services, where conventional anti-neuropathic pain agents AND conventional strong opioids (morphine or oxycodone) have failed to provide adequate pain relief or are not tolerated
- 2) **in pain without a neuropathic component:** under specialist direction from the pain services, where conventional strong opioids (morphine or oxycodone) have failed to provide adequate pain relief or are not tolerated.

Prescribers should refer to the **Guideline for the management of neuropathic pain** and **Adult pain management guidelines** (available on the [inpatient pain service](#) intranet page) for further information. Tapentadol should be treated like other opioid medications and co-prescription with other opioids should normally be avoided.

Prescriber Restrictions: For initiation by the pain services only (inpatient pain team, chronic pain team, or palliative care).

Primary Care Prescribing: The initial prescription will be provided by the specialist pain team, and response to this will be reviewed twice within 8-10 weeks after initiation. If treatment is to be continued, the GP will be asked to take over prescribing. A written medication plan will be provided by the pain specialist to support this, detailing the indication, dosage, formulation, titration guidance, expected duration, monitoring requirements, and arrangements for specialist pain team advice and/or follow-up.

Formulation: Prolonged-release tablets (Palexia® SR): 50 mg (white) (28-tab/ 56-tab packs); 100 mg (yellow) (56-tab pack); 150 mg (pink) (56-tab pack); 200 mg (orange) (56-tab pack) 250 mg (red) (56-tab pack).

Tapentadol is a Schedule 2 controlled drug (CD2) and therefore subject to full CD requirements relating to its prescription, safe custody and the need to keep registers.

Dosage Regimen: Prolonged-release tablets (Palexia® SR): initially 50 mg every 12 hours, adjusted according to response; max. 500 mg daily.

Unwanted Effects and Contraindications:

The adverse effect profile of tapentadol is similar to that of conventional opioids, including, for example, nausea and vomiting (particularly in initial stages), constipation, dizziness and somnolence. At higher doses, it may cause respiratory depression and reduced consciousness.

Tapentadol is contraindicated in patients who have hypersensitivity to tapentadol or any of its excipients. In common with other opioids, tapentadol is contraindicated in patients who have acute respiratory depression; depressed consciousness; head injury or raised intracranial pressure (opioid analgesics interfere with pupillary responses vital for neurological assessment); or are at risk of paralytic ileus.

Tapentadol should not be used in severe **renal impairment**. In significant **hepatic impairment**, do not exceed an initial maximum daily dose of 50 mg (with prolonged-release tablets). Tapentadol is not recommended for use during and immediately before labour and delivery. Limited data suggests tapentadol is excreted in breast milk, and therefore its use during breast feeding is not recommended.

Major Interactions:

Caution must be exercised in the co-prescription of tapentadol with other agents that affect synaptic neurotransmitter concentrations. The additive effects may cause adverse cardiovascular events (including hypertensive crisis) due to norepinephrine accumulation, or serotonin toxicity (tachycardia, hypertension, hyperthermia, altered mental state) due to serotonin accumulation.

In particular:

- Tapentadol must not be used in patients taking **monoamine oxidase inhibitors (MAOIs)** or those who have taken MAOIs within last 14 days, due to the risk of adverse cardiovascular events such as hypertensive crises.
- Caution must be exercised when considering the use of tapentadol in patients taking **drugs that effect serotonin reuptake** (e.g. tramadol, selective serotonin reuptake inhibitors, serotonin–noradrenaline reuptake inhibitors), due to the risk of serotonergic toxicity

Caution must be exercised when considering the use of tapentadol in patients taking **drugs that depress consciousness** such as benzodiazepines, barbiturates and other opioids, as the sedative effects may be additive. Dosage reduction (of tapentadol and/or the other agent) must be considered. Care must also be taken when combining tapentadol with mixed μ -opioid agonist/antagonists such as pentazocine, or partial μ -opioid agonists such as buprenorphine, which may interfere with the activity of tapentadol at the opioid μ -receptor.

Caution must be exercised when considering the use of tapentadol in patients taking drugs that are **strong inducers of hepatic enzymes** (e.g. rifampicin, phenobarbitone, St John's wort). The effect of tapentadol may be reduced during co-administration, and may increase following withdrawal of the enzyme inducer.

Advice to Patients: Patients must be:

- Warned about the effect of tapentadol on their ability to drive and use machinery
- Advised that tapentadol may enhance the effects of alcohol, which should ideally be avoided
- Asked to report any side effects to their GP or pain specialist, and to report if they become pregnant

Monitoring Including Criteria for Stopping:

Tapentadol has the potential for abuse and addiction. All patients treated with active substances that have opioid μ -receptor activity should be monitored carefully for signs of dependence/abuse/addiction, although in practice this is not usually a problem in therapeutic use.